

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet	1	of	7	Application Number	09/879,442
				Filing Date	June 11, 2001
				First Named Inventor	Vincent DUBOIS
				Group Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
				Attorney Docket Number	COUL-015/02US

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No.	Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
ADK	P1	4,277,466		Trouet et al.	07-07-1981
	P2	4,296,100		Baurain et al.	10-20-1981
	P3	4,376,765		Trouet et al.	03-15-1983
	P4	4,388,305		Trouet et al.	06-14-1983
	P5	4,639,456		Trouet et al.	01-27-1987
	P6	4,671,958		Rodwell et al.	06-09-1987
	P7	4,703,107		Monsigny et al.	10-27-1987
	P8	4,719,312		Firestone, R.A.	01-12-1988
	P9	4,870,162		Trouet et al.	09-26-1989
	P10	5,024,835		Rao et al	06-18-1991
	P11	5,220,001		Ok et al	06-15-1993
	P12	5,599,686		DeFeo-Jones et al.	02-04-1997
	P13	5,962,216		Trouet, et al.	10-05-1999

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Examiner Initials*	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Office	Number	Kind Code (if known)		
ADK	F1	BE	869 485	A		12-01-1978
	F2	BE	882 541	A		07-16-1980
	F3	EP	0 037 388	B1	INSTITUT INTERNATIONAL DE PATHOLOGIE CELLULAIRE ET MOLECULAIRE	03-30-1981
	F4	EP	0 041 935	A1	OMNICHEM	12-16-1981
	F5	EP	0 044 090	A2	MERCK & CO.	01-20-1982
	F6	EP	0 126 344	A2	ABBOTT LABORATORIES	11-28-1994
	F7	EP	0 126 685	A1	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	11-28-1984
	F8	EP	0 208 615	B1	IRE-CELLTARG	01-14-1987
	F9	EP	0 475 230	A1	BRUNSWICK CORPORATION	09-02-1991
	F10	EP	0 640 622	A1	DRUG DELIVERY SYSTEM INSTITUTE, LTD.	02-29-1994
	F11	WO	92/07068	A1	ATHENA NEUROSCIENCES, et al.	04-30-1992
	F12	WO	93/02703		IGEN, INC.	02-18-1993
	F13	WO	96/00503		MERCK & CO., INC.	01-11-1996
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	F15	WO	96/33198	A1	DRUG INNOVATION & DESIGN, INC.	10-24-1996
	F16	WO	98/52966	A1	THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE	11-26-1998
	F17	WO	00/33888	A2	COULTER PHARMACEUTICALS, INC., et al	06-15-2000

Examiner Signature	<i>ADK</i>	Date Considered	10/25/04
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OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
ADK	D1	ABOLD-PIRAK, Esther, et al., "Cytotoxic activity of Daunorubicin or Vindesin Conjugated to a Monoclonal Antibody on Cultured MCF-7 Breast Carcinoma Cells," <i>Biochem. Pharmacol.</i> 38:641-648 (1989)	
	D2	BALAJTHY et al., "Synthesis and Functional Evaluation of a Peptide Derivative of 1-β-D-Arabinofuranosylcytosine," <i>J. Med. Chem.</i> 35:3344-3349 (1992)	
	D3	BARRETT, AJ, et al., (eds.) "Thimet oligopeptidase." <i>Handbook of proteolytic enzymes</i> (with cd-rom). [371], 1108-1111. 1998. San Diego, Academic Press.	
	D4	BARRETT, et al., "Thimet Oligopeptidase and Oligopeptidase M or Neurolysin [32]," <i>Meth. Enzymol.</i> 248:529-556 (1995)	
	D5	BARRETT, et al., "Chicken liver Pz-peptidase, a thiol-dependent metallo-endopeptidase," <i>Biochem J</i> 271:701-706 (1990)	
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	D7	BAURAIN, et al., "Antitumor Activity of Daunorubicin Linked to Proteins: Lysosomal Hydrolysis and Antitumor Activity of Conjugates Prepared with Peptidic Spacer Arms," <i>Chemical Abstracts</i> 97:386 (1982)	
	D8	BAURAIN, et al., "Antitumor Activity of Daunorubicin Linked to Proteins: Lysosomal Hydrolysis and Antitumor Activity of Conjugates Prepared with Peptidic Spacer Arms," <i>Curr. Chemother. Immunother., Proc. Int. Congr. Chemother., 12th</i> (1982), Vol. 2, 1430-32 (1982)	
	D9	BAURAIN, et al., "Targeting of Daunorubicin by Covalent and Reversible Linkage to Carrier Proteins. Lysosomal Hydrolysis and Antitumoral Activity of Conjugates Prepared with Peptidic Spacers." <i>Drugs Exp. Clin., Vol. 9</i> , pp 303-311, 1983	
	D10	BRICOUT, Herve, et al., "Synthetic and Kinetic Aspects of Nickel-Catalysed Amination of Allylic Alcohol Derivatives," <i>Tetrahedron</i> 54:1073-1084 (1998)	
	D11	BUCHLER, M, et al. "Proteinase yscD (oligopeptidase yscD). Structure, function and relationship of the yeast enzyme with mammalian thimet oligopeptidase (metalloendopeptidase, EP 24.15)," <i>Eur.J.Biochem.</i> 219:627-639 (1994)	
	D12	CAMARGO, AC, et al. "Structural requirements of bioactive peptides for interaction with endopeptidase 22.19," <i>Neuropeptides</i> 26:281-287 (1994)	
	D13	CARDOZO, C, et al. "Evidence that enzymatic conversion of N-[1(R,S)-carboxy-3-phenylpropyl]-Ala-Ala-Phe-p-aminobenzoate, a specific inhibitor of endopeptidase 24.15, to N-[1(R,S)-carboxy-3-phenylpropyl]-Ala-Ala is necessary for inhibition of angiotensin converting enzyme," <i>Peptides</i> 14:1259-1262 (1993)	
	D14	CASALE, L, et al. "Quantitation of endopeptidase 24.11 and endopeptidase 24.15 in human blood leukocytes," <i>Enzyme Protein</i> 48:143-148 (1994)	
ADK	D15	CHAIRES, et al., "Self-Association of Daunomycin," <i>Biochemistry</i> 21:3927-32 (1982)	

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Examiner Name	Not Yet Assigned
Attorney Docket Number	COUL-015/02US

Sheet	3	of	7
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D16	CHAKRAVARTY et al., "Plasmin-Activated Prodrugs for Cancer Chemotherapy. 1. Synthesis and Biological Activity of Peptidylacivicin and Peptidylphenylenediamine," <i>J. Med. Chem.</i> 26:633-638 (1983)
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D18	CHEN, et al., "Immunolocalization of thimet oligopeptidase in chicken embryonic fibroblasts," <i>Exp. Cell Res</i> 216:80-85 (1995)
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D21	CRACK, et al., "The association of metalloendopeptidase EC 3.4.24.15 at the extracellular surface of the AtT-20 cell plasma membrane," <i>Brain Res</i> 835:113-124 (1999)
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D23	DE MARRE, et al., "Evaluation of the hydrolytic and enzymatic stability of macromolecular Mitomycin C Derivatives," <i>J. Controlled Release</i> 31:89-97 (1994)
D24	DELUCIA, et al., "Efficacy and toxicity of differently charged polycationic protamine-like peptides for heparin anticoagulation reversal," <i>J. Vasc. Surg.</i> 18:49-60 (1993)
D25	DUBOIS, et al., "Pharmacokinetics and Tissue Distribution of CPI-004, a New Prodrug of Doxorubicin, in Normal and Tumor-Bearing Mice." Abstract #3329, American Association for Cancer Research, Scientific Proceedings, April 1-5, 2000.
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D28	FERRO, et al., "Secretion of a neuropeptide-metabolizing enzyme similar to endopeptidase 22.19 by glioma C6 cells," <i>Biochem. Biophys. Res. Commun.</i> 191:275-281. (1993)
D29	FERRO, et al., "Secretion of metalloendopeptidase 24.15 (EC 3.4.24.15)," <i>DNA Cell Biol</i> 18:781-789 (1999)
D30	GARRIDO, et al., "Confocal microscopy reveals thimet oligopeptidase (EC 3.4.24.15) and neurolysin (EC 3.4.24.16) in the classical secretory pathway," <i>DNA Cell Biol</i> 18:323-331 (1999)
D31	GENET, et al., "A General and Simple Removal of the Allyloxycarbonyl Protecting Group by Palladium-Catalyzed Reactionos Using Nitrogen and Sulfur Nucleophiles," <i>Synlett</i> 680-682 (1992)

Examiner Signature	<i>ADL</i>	Date Considered	06/25/04
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First Named Inventor	Vincent DUBOIS
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Examiner Name	Not Yet Assigned

D32	GENET, et al., "Practical Palladium-Mediated Deprotective Method of Allyloxycarbonyl in Aqueous Media," <i>Tetrahedron</i> . Vol. 50, No. 2 497-503 (1994)
D33	GLUCKSMAN and ROBERTS, "Strategies for characterizing, cloning, and expressing soluble endopeptidases," <i>Methods in Neurosciences</i> , 23: 296-316 (1995)
D34	HARNOIS-PONTONI, I. et al., "Hydrosoluble Fluorogenic Substrates for Plasmin" <i>Analytical Biochemistry</i> , 193, 248-255 (1991)
D35	HAYASHI, et al. "Species specificity of thimet oligopeptidase (EC 3.4.24.15)," <i>Biol.Chem Hoppe-Seyler</i> 377:283-291 (1996)
D36	HOES and FEIJEN "The Application of Drug-Polymer Conjugates in Chemotherapy" in <i>Horizons in Biochemistry and Biophysics Vol. 9: Drug Carrier Systems</i> , pp. 57-109 (1989)
D37	ISRAEL, M. et al., "Adriamycin Analogues. Preparation and Biological Evaluation of Some N-(Trifluoroacetyl)-14-O-[(N-acetyl amino)acyl] adriamycin Derivatives" <i>J. of Med. Chem.</i> , 1986, Vol. 29, 1273-1276
D38	JACCHIERI, et al. " comparative conformational analysis of thimet oligopeptidase (EC 3.4.24.15) substrates," <i>J. Pept.Res</i> 51:452-459 (1998)
D39	JIRACEK, et al. "Development of highly potent and selective phosphinic peptide inhibitors of zinc endopeptidase 24-15 using combinatorial chemistry." <i>J. Biol. Chem</i> 270:21701-21706 (1995)
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D41	KATO, et al., "Cloning, amino acid sequence and tissue distribution of porcine thimet oligopeptidase. A comparison with soluble angiotensin-binding protein," <i>Eur J Biochem</i> 221:159-165 (1994)
D42	KENNETT et al., "Comparative Histochemical, Biochemical and Immunocytochemical Studies of Cathepsin B in Human Gingiva," <i>Chem. Abstr.</i> , 121:79924, 1994
D43	KING, et al., "Synthesis and proteolytic cleavage of 3'-N -peptidyl-Adriamycin prodrugs," <i>Struct. Biol.</i> 137-139 (1988)
D44	KNIGHT and BARRETT, "Structure/function relationships in the inhibition of thimet oligopeptidase by carboxyphenylpropyl-peptides," <i>FEBS Lett</i> 294: 183-186 (1991)
D45	KNIGHT, et al. "Thimet oligopeptidase specificity: evidence of preferential cleavage near the C-terminus and product inhibition from kinetic analysis of peptide hydrolysis," <i>Biochem.J.</i> 308:145-150 (1995)
D46	KRAUSE, et al., "Characterization and localization of mitochondrial oligopeptidase (MOP) (EC 3.4.24.16) activity in the human cervical adenocarcinoma cell line HeLa," <i>J Cell Biochem</i> 66:297-308 (1997)
D47	LESSER, et al. "Hydrolysis of N-formylmethionyl chemotactic peptides by endopeptidase 24.11 and endopeptidase 24.15," <i>Peptides</i> 17:13-16 (1996).

Examiner Signature	<i>Ph 08</i>	Date Considered	10/25/04
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ADK	D48	LEW, et al. "Evidence for a two-step mechanism of gonadotropin-releasing hormone metabolism by prolyl endopeptidase and metal loendopeptidase EC 3.4.24.15 in ovine hypothalamic extracts," <i>J. Biol. Chem.</i> 269:12626-12632 (1994)	
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	D50	MASQUELIER, et al., "Amino Acid and Dipeptide Derivatives of Daunorubicin, 1. Synthesis, Physicochemical Properties, and Lysosomal Digestion," <i>J. Med. Chem.</i> 23:1166-1170 (1980)	
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	D53	MATZANKE, et al., "Evidence for Polynuclear Aggregates of Ferric Daunomycin," <i>Eur. J. Biochem.</i> 207:747-55 (1992)	
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	D55	MCKIE, N, et al. "Rat thimet oligopeptidase: large-scale expression in <i>Escherichia coli</i> and characterization of the recombinant enzyme," <i>Biochem.J.</i> 309:203-207 (1995)	
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	D57	MOODY, et al., "Neurotensin is metabolized by endogenous proteases in prostate cancer cell lines," <i>Peptides</i> 19:253-258 (1998)	
	D58	MORALES, et al., "PZ-peptidase from Chick Embryos. Purification, Properties, and Action on Collagen Peptides," <i>J Biol Chem</i> 252:4855-4860 (1977)	
	D59	NOBLE, et al., "Association of aminopeptidase N and endopeptidase 24.15 inhibitors potentiate behavioral effects mediated by nociceptin/orphanin FO in mice," <i>FEBS Lett.</i> 401:227-229 (1997)	
	D60	OLIVEIRA, et al., "Characterization of thiol-, aspartyl-, and thiol-metallo-peptidase activities in madin-darby canine kidney cells," <i>J Cell Biochem</i> 76:478-488 (2000)	
	D61	ORLOWSKI, et al. "Substrate-related potent inhibitors of brain metalloendopeptidase." <i>Biochemistry</i> 27:597-602 (1988)	
	D62	ORLOWSKI, et al., "Endopeptidase 24.15 from rat testes. Isolation of the enzyme and its specificity toward synthetic and natural peptides, including enkephalin-containing peptides," <i>Biochem J</i> 261:951-958 (1989)	
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D64	PINEAU, et al. "Distribution of thimet oligopeptidase (E.C. 3.4.24.15) in human and rat testes," <i>J. Cell Sci</i> 112:3455-3462 (1999)	
D65	POZGAY, et al. "Substrate and Inhibitor Studies of Thermolysin-like Neutral Metallopeptidase from Kidney Membrane Fractions: Comparison with Bacterial Thermolysin," <i>Biochem.</i> 25:1292-1299 (1986)	
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D72	SHAPIRO, et al., "Mild and Rapid Azide-Mediated, Palladium Catalyzed Cleavage of Allylester Based Protecting Groups," <i>Tetrahedron</i> 35:5421-5424 (1994)	
D73	SHRIMPSON, et al., "Thiol Activation of Endopeptidase EC 3.4.24.15," <i>J. Biol. Chem.</i> 272:17395-17399 (1997)	
D74	TABRIZI-FARD, et al., "Evaluation of the Pharmacokinetic Properties of a Doxorubicin Prodrug in Female ICR(CD1) Mice Following Intravenous Administration," <i>Proc. Amer. Assoc. Cancer Res.</i> , 42:324 (2001)	
D75	TAYLOR & AMIDON (eds.) <i>Peptide-Based Drug Design, Controlling Transport and Metabolism</i> , 1995, 423-445, 449-467 (2 chapters)	
D76	THOMPSON, et al. "Cloning and functional expression of a metalloendopeptidase from human brain with the ability to cleave a beta-APP substrate peptide," <i>Biochem Biophys Res Commun</i> 213: 66-73 (1995)	
D77	TISLJAR and BARRETT "Thiol-dependent metallo-endopeptidase characteristics of Pz-peptidase in rat and rabbit," <i>Biochem J</i> 267: 531-533 (1990)	
D78	TISLJAR, "Thimet oligopeptidase—a review of a thiol dependent metallo-endopeptidase also known as Pz-peptidase endopeptidase 24.15 and endo-oligopeptidase," <i>Biol Chem Hoppe Seyler</i> 374: 91-100 (1993)	
D79	TRAIL, P.A., et al., "Cure of Xenografted Human Carcinomas by BR96-Doxorubicin Immunoconjugates" <i>Science</i> Vol. 261, 9 July 1993, 212-215	

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ADK	D80	TROUET, et al., "A covalent linkage between daunorubicin and proteins that is stable in serum and reversible by lysosomal hydrolases, as required for a lysosomotropic drug-carrier conjugate: In Vitro and vivo studies," <i>Proc. Natl. acad. Sci. USA</i> 79:626-629 (1982)	
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	D86	WAKEFIELD, et al., "Heparin-mediated reductions of the toxic effects of protamine sulfate on rabbit myocardium," <i>J. Vasc. Surg.</i> 16:47-53 (1992)	
	D87	WALDMANN, et al., "Synthesis of the Palmitoylated and Prenylated C-Terminal Lipopeptides of the Human R- and N-Ras Proteins," <i>Bioorg. Med. Chem.</i> 7:749 (1998)	
	D88	WALDMANN, and SEBASTIAN, "Enzymatic Protecting Group Techniques," <i>Chemical Reviews</i> , 94:911-937 (1994)	
	D89	WANG, "p-Alloxybenzyl Alcohol Resin and p-Alkoxybenzyloxycarbonylhydrazide Resin for Solid Phase Synthesis of Protected Peptide Fragments," <i>J. Am. Chem. Soc.</i> 95:1328 (1973)	
	D90	WHALLEY, "Receptors Mediating the Increase in Vascular Permeability to Kinins: Comparative Studies in Rat, Guinea Pig and Rabbit," <i>Chem. Abstr.</i> , #107: 127965, 1987	
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ADK	D93	MASQUERLIER, et al., "Incorporation and Binding of Anthracycline Derivatives to Low Density Lipoprotein: In vitro and in vivo Studies of Drug-LDL Conjugates," Recent Adv. Chemother., Proc. Int. Congr. Chemother., 14 th Volume, Anticancer Section 1, pp. 311-12 (1985)	

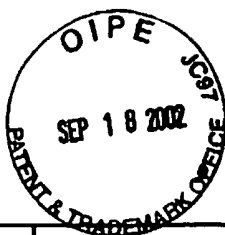
¹ Unique citation designation number.² Applicant is to place a check mark here if English language Translation attached.

Examiner Signature	<i>AK</i>	Date Considered	10/25/04
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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09/879,442 on 07/21/2004



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Substitute for form 1449A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				TRADE MARK Complete if Known		RECEIVED
				Application Number	09/879,442	
				Filing Date	June 11, 2001	SEP 20 2002
				First Named Inventor	Vincent DUBOIS	
				Group Art Unit	1646	
				Examiner Name		
Sheet	1	of	1	Attorney Docket Number	COUL-015/02US	TECH CENTER 1800/290

[illegible]

Examiner Signature		Date Considered	10/25/04
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² Applicant is to place a check mark here if English language Translation attached.